NANO COSMETICS: UNDERSTANDING RISKS AND TOXICITY OF NANOMATERIALS

Rajkumar S Moon*, Chaitanya R Awale, Shubham D Powar, Amarnath B Pawar,
Dattatrya D Aradwad, Yuvraj R Navkhande

School of Pharmacy, S.R.T.M. University, Nanded, Maharashtra, India - 431606

* **Corresponding Author**
Dr. Rajkumar S. Moon
Assistant Professor
School of Pharmacy
S.R.T.M.University, Nanded,
Maharashtra, India- 431606

ABSTRACT

The term "nano cosmetics" refers to a class of cosmetics that incorporate nanoparticles (NPs), which have been applied in a variety of scientific and technological domains. Nanotechnology involves manipulating materials and creating structures and systems at nanoscale, with applications in pharmaceutical sciences and the cosmetic industry. It involves design, characterization, and production of nanoparticles at nanometre scales without neglecting safety and efficacy. However, the European Scientific Committee on Consumer Safety (SCCS) has not yet assessed the risk of nano-sized colloidal gold (Au) and silver (Ag) in oral and cutaneous cosmetic products. Polymeric capsules called nano capsules, dendrimers, and fullerenes are used in cosmetics to preserve active ingredients, lessen odours, encourage permeation, and improve bioavailability and biocompatibility. This article focusses on the uses of nanomaterials and the safety and toxicity evaluation of nanoparticles (nano-titanium oxide, nano-zirconium, nano-gold, nano-aluminium, and nano-silica) in cosmetics. Additionally, it provides an overview of the current status of nanotechnologies in the cosmetics sector, regulatory authorities, and their role. The safety assessment parameters of nano cosmeceutical such as sensitization, irritation to eyes and skin, permeability, genotoxicity, carcinogenicity are discussed. The routes of exposure of nano cosmetics into the human body which facilitate the entry in the body are highlighted. The toxicity that the human body experiences is caused by the possible nanomaterials. Toxicity of nanomaterials is due to their extremely small size which allow them to be readily absorbed into biological systems. Once inside the body they can accumulate in organ, cross biological barriers and interfer with cellular functions.

KEYWORDS: Nano-materials, Nano-cosmetics, Safety assessment, Regulatory compliance.

INTRODUCTION

The processes involved in manipulating materials and building systems and structures at the nanoscale are referred to as nanotechnology. Since it first emerged as a potent fundamental and applied science instrument, this discipline has been in the spotlight in the pharmaceutical research and development and cosmetic industry sectors. Nanotechnology is defined by the National Nanotechnology Initiative (1) as study and technological development at the atomic, molecular, or macromolecular levels on the length range of about 1 to 100 nanometres.

The Parallel field called as nanobiotechnology which introduces the biological properties such as nano medicine, biomedical and agriculture. Nanotechnology consists of design, production, characterization and to keep control on size and shape at nanometer scale without neglecting the safety and efficacy.

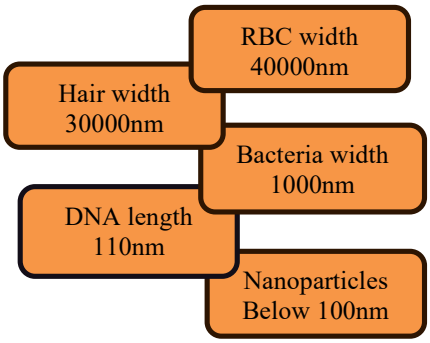

Fig. 1: Understanding nanoparticles size

Through modification of the physiochemical characteristics of nanoparticles, we can enhance their absorption and engagement with biological tissue. The active components are really shielded from deterioration before distribution at a regulated rate and time (2).

APPROACHES AND APPLICATIONS OF NANOPARTICLES

Fig. 2 Approaches of nanoparticles

Liposomes

Liposomes below 100 nm are called as nano liposomes. Liposomes are circular two-layered vesicles with an aqueous volume enclosed by a phospholipid bilayer (3). The advantages of nano liposomes are that they are biodegradable and biocompatible. liposomes play very crucial role by protecting the active ingredient. Because of its modest size, the surface area of nano liposomes is bigger and their stability profile satisfactory at the nanometric scale, such as for small liposomes 20–100 nm size and for large liposomes >100 nm size (4). Lipsticks, body spray deodorants and antiperspirants can all benefit from their ability to convey aroma. The restricted usage in cosmetics is caused by problems with physicochemical instability, poor drug loading and low repeatability (3).

Solid lipid Nanoparticles (SLNs)

Because of their many benefits over the current traditional formulation, they serve as a carrier for chemicals and are quite efficient in moisturising the skin (5). The single-layer shells that make up SLNs have an oily or lipoidal core (6). Because SLNs are small, they can effectively touch the stratum corneum, enhancing the chemicals' ability to pass through the skin (7). In addition to potentially serving as UV blockers, they can increase the skin's moisture level. While SLNs might increase chemical stability, NLCs (Nanostructured lipid carrier) can contain more active chemicals (8). They demonstrate skin penetration, stability enhancement, and biocompatibility as an efficient carrier delivery agent (9). Sunscreens and moisturising creams include SLNs and NLCs (3).

Table 1: Products containing solid lipid nanoparticles

Name of the product	Marketed by	Applications
Allure Body Cream	Chanel	Moisturiser
Allure Perfume	Chanel	Fragrance
Allure Eau Perfume	Chanel	Fragrance

Nano-emulsion

Nano emulsions are often defined as W/O or O/W colloidal dispersions including droplets with a diameter range is from some nanometres to 200 nm (10). In contrast to traditional emulsions, the small size of droplet can aid in achieving the appropriate rheological, qualities of stability, optical quality, and ingredient delivery. Nano emulsions are clear and stable. Opuntia ficus-indica (L) Mill hydro glycolic extract used to produce an O/W nano-emulsion, and its moisturising and thermal stability were assessed (11). According to the results, nano emulsions with 1% extract of Opuntia ficus-indica (L) Mill were stable for at least two months. By improving its moisturising ability, the formulation even managed to increase the water content of the stratum corneum. In particular, compared to traditional emulsions, O/W Nano-emulsions greatly enhanced the penetration profiles of nonpolar components (3).

Table 2: Marketed nano emulsions (12)

Drug	Brand	Indication
Propofol	Diprivan®	Anaesthetic
Dexamethasone	Limethason®	Steroid
Flurbiprofen axetil	Ropion®	NSAID
Fat soluble vitamins	Vitalipid®	Intravenous nutrition

Nano-gold

Apart from their numerous applications, gold (Au) and silver (Ag) nanoparticles have antibacterial and antifungal properties as well (13). Deodorants and anti-aging creams are examples of cosmetics that contain Au and Ag nanoparticles. The safety of colloidal Au and Ag at nanoscale levels in oral and topical cosmetic products has not yet been decided by the European SCCS (14). Since cosmetics' claims of antibacterial properties are based on physiological functions, they are not allowed in the United States and are limited to pharmaceutical products (15). According to studies on the applications of Au and Ag nanoparticles in cosmetic designs, Ag nanoparticles agglomerate

after being incorporated into cream mixtures, but Au nanoparticles did not. According to a model dermal membrane investigation, they raised worries about the capacity of nanoparticles at dosages of 110–200 mg/kg to pass through the skin (16).

Nano-capsules

In 1988, L'Oréal released "Plenitude Revitalift," the first nano capsule carrying an anti-aging cream (17). These capsules are made of polymers and have an oily or watery core. The polymeric membranes have a liquid or solid core (18), and the liquid and solid lipids that comprise the cosmetic ingredients are found in the core. Many different hydrophilic and hydrophobic compounds can be held by these nanoparticles. However, their primary function is to enhance the action of chemically unstable chemicals like antioxidants and tretinoin, as well as organic components which are partially water soluble and volatile components like aromatic molecules (19). By preserving active chemicals, reducing odours, promoting penetration, offering high physical stability, regulating the release of active ingredients, and enhancing the bioavailability and biocompatibility of the active components, nano capsules are utilized in cosmetics to indirectly improve skin protection (6).

Fullerene

Functionalized fullerenes have been a part of cosmetics for over more than ten years, since 2005 fullerene NPs have been marketed in cosmetics. C60 is the most popular type of fullerene. Because of its neuroprotective effects, enzyme inhibition, antibacterial, antiviral, and antifungal qualities, as well as its targeted drug delivery and diagnostic capabilities, C60 has applications in biomedicine. Recently, due to excellent penetration properties and moisturizing effects the sustainable environment friendly and naturally derived fullerene had developed. (20). Fullerene not only protects the skin from UV radiation but also enhances its antioxidant capacity. Promising outcomes were observed in in-vitro experiments where various human dermal cells were treated with fullerene derivatives prior to, during, or following UV radiation. Additionally, it may brighten the complexion by controlling the synthesis of melanin and preventing the generation of free radicals, and it can protect the skin by decreasing keratinocyte differentiation. Because of its excellent antioxidant and antibacterial properties, it has become increasingly widely used in skin repair and anti-aging products (21).

Dendrimers

The main factor contributing to dendrimers' versatility is its spherical structure, this consists of a core around which symmetric units are build (22). Polymers called dendrimers are very stable and facilitate the delivery of materials through the skin's layers (8). Dendrimer symmetrical branches' surface activity is provided by the hydrophilic core and hydrophobic edge parts of the dendrimers

(23). Their stability, polyvalence, and mono-dispersity make them perfect drug delivery vehicles (6). Because of its anti-oxidant and anti-aging qualities, resveratrol's total loading and skin penetration ability are enhanced by dendrimer structure (24).

Table 3: Products containing dendrimers (25)

Category	Brand name	Application
Diagnostic agent	Stratus	Cardiac biomarkers Measurement
Transfection agent	Superfect®	Cell transfection
Contraceptive	VivaGel®	Prevention of STI
Therapeutic agent	VivaGel BV®	Antiviral agent

ROUTES OF EXPOSURE

Ingestion

The bulk of toxicity studies pertinent to NPs are mostly focused on exposures to the respiratory tract (RT), and very few literatures cover exposures to NPs in the gastrointestinal tract (GI). Hand-to-mouth transfers and conventional materials are the most common causes of unintentional exposures to the gastrointestinal tract (GI). The nanomaterials which are present in lipstick and the nail polish have more chances to get ingest through the mouth and reach to the gastrointestinal tract. Additionally, it could happen while handling products that include nanoparticles. The mucociliary escalator removes the particles from the respiratory system may expose the gastrointestinal tract (GI) to additional potential hazards (26). Moreover, nanomaterials included in food, drink, cosmetics, medications, and drug delivery systems can enter the GI system. According to studies by Jani (1990), compared to the titanium particles typically found in sunscreen, particles between 150 and 500 nm in size have a higher chance of entering the lymphatic, hepatic, and splenic systems through the gastrointestinal tract. Due to smaller in size nanomaterials may easily penetrate BBB and may affect the functions of brain. Studies on radioactive metals have provided more important information about the fate of ingested nanoparticles (NPs), as it has been demonstrated that NPs can go from the gastrointestinal tract to other organs (27).

Dermal exposure

The epidermis and dermis, the outer two layers of the skin, are the biggest organs in the body and serve as the body's contact with the outside environment, an insulator, a source of vitamin D, and a barrier against external influences. Cuts, scrapes, and dermatitis are examples of changes in the skin barrier that might allow nanoparticles (NPs) to enter the body and should not be neglected. Nanoparticles may be easier to penetrate the skin and enter the systemic circulation if formulations like lotions,

moisturizers, and sunscreens with nanoparticles are applied to the skin often. Skin that has been damaged provides an excellent entry point for both smaller and larger particles (0.5-7µm) as reported (28). According to research from North Carolina State University, skin abrasion caused quantum dot nanoparticles to penetrate the skin. This raises concerns about worker safety resulting from occupational activities, particularly for those involved in the manufacturing of quantum dots and other NPs (29). Results indicate that nanoparticles (NPs) with a diameter of less than 1 µm can mechanically pierce skin (30). Recent studies have demonstrated that quantum dot (QD621) NPs, NPs with cadmium and selenium core with cadmium sulphite, can penetrate the skin when applied topically to the skin of weaning Yorkshire pigs **(31).**

Ocular exposure

There aren't many reports and literature suggesting that NPs enter animals through the eyes. Topical application is the method used to give medication (32). However, topical treatment of posterior eye infections is beneficial due to the corneal epithelial impermeability, increased lacrimation, long diffusional channel length, and rapid peroneal elimination caused by solution drainage (33). However, because of their capacity to deliver drugs directly into the eye, NPs are attracting a lot of attention (32).

Respiratory exposure

The toxicity of NPs to the respiratory system has been the subject of several investigations. In order to conduct toxicity research, these nanomaterials can be intentionally injected into the respiratory system or inhaled spontaneously as aerosols or powders (34). For example, research indicates that when assessing the toxicity of NPs in animals' respiratory tracts, they can be administered intraperitoneally, oropharyngeally, or intrapharyngeally (35). The respiratory tract includes the lungs, which are in charge of gas exchange. Upper respiratory tract the most typical way that people are exposed to NPs at work is by inhalation. These substances travel to the lower respiratory tract through the electrostatic force of the air after being inhaled (34). The particles are usually ingested as airborne particulates (NPs) or systemically delivered medications, chemicals, and other substances because they enter the lungs through the pulmonary arteries directly from the heart (36). The discovery of quantum dots (10 nm) in the experimental mouse's liver, lymph, and bone marrow gave this study more credibility. Relying on the size of the nanomaterial, transfer to blood circulation via lymphatic channels may occur as soon as the NPs reach the pulmonary locations (37).

POTENTIAL TOXIC NANOMATERIALS USED IN NANO COSMETICS

Usually, organic or inorganic chemicals serve as the basis for nanomaterials utilized in cosmetics. Organic-based nanoparticles consist of lipid and polymeric systems, while inorganic-based nanoparticles are composed of metals. The composition, physicochemical characteristics and bio

interaction of nanoparticles determine their toxicity. When makeup is applied, the skin comes into contact with a number of formulation ingredients, including any nanoparticles that may be present and which have varying degrees of toxicity. Therefore, while investigating various cosmetics containing nanoparticles, related hazards of nontoxicity need to be kept in mind.

Nano-Titanium dioxide

Titania is another name for titanium dioxide. Its many different actions have led to its widespread use. It is typically utilized as colors in creams and lotions, as well as for UV radiation screening in sunscreen and loose powders. Its basic function is to deflect UVB (290–320 nm) and UVA (320–400 nm) radiations, which are the main contributors to skin tumor malignancy (38). As a pigment, it scatters sunlight to give optical protection. This is accomplished by applying a thin coating of formulation to the areas that need to be protected, such as the lips or skin. Rutile, ilmenite, and anatase are the three distinct crystalline forms of titanium dioxide (39). Additionally, anatase form of titanium dioxide can cause cellular dysfunctions in human glial cells and lung cells cultivated in vitro, such as oxidative stress, cell death, and decreased mitochondrial activity (40). Along with chromosome abnormalities in the human gut, it can also result in contacts between nuclei and break DNA strands. Because of their ability to reject water or stains, nanoscale compounds including alumina or silica are commonly used to completely cover TiO2 in order to reduce its photocatalytic properties (2).

Nano-Gold

Gold (Au) has been used in cosmetics in a number of applications, such as creams, packs, and direct application foils. Gold nanoparticles are utilized to improve skin tone, speed up blood circulation, and revitalize the skin's fiber tissues. It has become intriguing to look at the uses of nanoparticles of gold in skin care products since, according to continuing cancer research, they aid in the destruction of cancerous cells in the body. Due to their higher LD50 or LD80 values, nano sized gold colloids are seen to be rather inert toward biological systems (41). However, biodegradability, whether in the form of individual particles or aggregates raises serious questions regarding their long-term circulation in plasma and accumulation in cells. Based on data showing that gold nanoparticles may readily aggregate in lung cells, an in vitro experiment was conducted using A549 lung cells (42). 1.4 nm-sized gold nanoparticles are capable to cause oxidative stress, necrosis, and mitochondrial damage (43).

Nano-Zirconium oxide

The metal zirconium is silver-gray. It shares many of the same properties as titanium, including being extremely strong, ductile, shiny and corrosion and heat resistant. Zirconium-containing

complexes have been utilised in cosmetics as antiperspirants and deodorants (47). In its aerosolized form, zirconium can pass through the placental and blood brain barriers as well as the interior regions of the lungs. Zirconium oxychloride is mutagenic in vivo and clastogenic in vitro, according to genome toxicity studies (48). Agents known as clastogenic chemicals cause chromosomal integrity or arrangement disruptions or alterations. According to Section 601(a) of the Federal Food, Drug, and Cosmetic Act, any zirconium-containing cosmetic aerosol is deemed adulterated and is subject to regulatory action for interstate commerce. Although nanoscale zirconium dioxide is utilized as an opacifier, fibroblasts and macrophages have been shown to be harmful to particles larger than 530 nm (49).

Nano-Silica

It has been shown that silica is the most primordial mineral that humans have found. Despite having varying atomic configurations, all types of silica contain the same chemical makeup. Both crystalline and amorphous forms of silica exist. Lung cancer, silicosis, and other lung disorders are brought on by crystalline silica (44). In nature, amorphous forms may be found in granite, sandstone, and clay, as well as in some plants that exhibit corrosive and irritating properties as well as dermal and percutaneous absorption. Since the porous spheres in silica may release aroma for a longer amount of time, silica is also utilized as a component in powdered perfume. It contains antiallergenic, antihistamine, immunosuppressive, hypocholesterolemia, and antiapoptotic properties in addition to its cosmetic advantages (45). According to in vitro research, silica nanoparticles harm DNA by producing reactive oxygen species (ROS) upon endocytosis. When nano silica builds up, protein aggregates and nuclear inclusions are formed and membrane disruption which leads to both the cell cycle and apoptosis arrest (46). Even at greater dosages (200–500), particles larger than 60 nm might be more harmful than smaller ones and only create reactive oxygen species (ROS). However, particles smaller than 20 nm have the potential to harm intercellular structures.

Nano-Aluminium

Al2O3, or aluminum oxide, is the chemical formula for this inorganic mixture of aluminum and oxygen. Aluminum oxide nanoparticles have been used as additives and fillers in cosmetics recently. Because of its stability, antibacterial qualities, nontoxic profile, and high adsorption capacity, its applications have been growing throughout the last several years. Aluminum oxide nanoparticles' cytotoxic effects on two distinct mammalian cell lines, L929 and BJ, were investigated by E Radziun et al. using the EZ4U assay. A mitochondrial enzyme known as succinate dehydrogenase's activity was assessed, and it was discovered that the oxide nanoparticles had a minimal, less than 10% cytotoxic effect (50). It's interesting to note that hydrated aluminum oxides, which are found in

toothpastes as particles and dispersants, can be exposed orally through toothpastes. Sun protection products, nail polish, and face masks commonly include aluminum oxide nanoparticles. Another study addressed the negative effects of inhaling alumina nanoparticles using RAW 264.7 macrophage cells based on three parameters: the formation of ROS, lactate dehydrogenase release, and the alpha tumour necrosis factor. It was found that the nanoparticles exhibited no noticeable cytotoxicity when compared to the positive control (2).

SAFETY CONSIDERATIONS

Nanomaterial-based cosmetics can be used for a number of reasons. (e.g., sunscreens with UVA and UVB filters, nano-preservatives). The unique characteristics of each individual nanomaterial that could lead to the intended activity or characteristic of the cosmetic product could put the consumer at risk. This implies that all nanomaterials must go through a safety evaluation that involves assessing their nano-characteristics (e.g., inhalation tests for sprays or powders, or the capacity to penetrate viable skin layers due to their tiny size). The FDA's most recent recommendations state that the safety evaluation should include a number of crucial factors, including the NMs' physicochemical characteristics, aggregation, and size distribution, as well as their form, solubility, density, porosity, stability, and contaminants (51).

REGULATORY CONSIDERATIONS

General regulatory considerations

The cosmetics industry is a dynamic, expanding worldwide industry. Massive industry innovation over the last few decades has led to a rise in sales and a wide range of new items. At a compound annual growth rate of 5.1% from 2021, the worldwide cosmetics industry is predicted to reach USD 560.50 billion by 2030 from its 2020 valuation of USD 341.1 billion (52). To guarantee the safety and quality of cosmetic products and prevent harmful effects on the health of consumers, the cosmetics sector must be regulated. This is because the industry is very innovative, dynamic, and complex. It is highly challenging for a multinational corporation to provide the same product everywhere, nevertheless, because national and market regulatory systems are far from aligning (53). There are still enough variances across the major markets' regulatory frameworks, despite their overall similarity, to have an impact on the sector by limiting innovation and decreasing market development potential. International trade may also be impacted by these differences and make it more challenging for regulatory agencies to guarantee that all items adhere to national and international standards (54).

Current Regulatory System:

The worldwide cosmetics industry has experienced substantial growth in recent years. Given the widespread use of social media as well as online purchasing, which have simplified the process of product advertising globally, effective marketing is essential in this fiercely competitive industry. The global trade of cosmetics industry is highly advantageous, as it guarantees equal accessibility to products for all, fulfills consumer demands, and encourages growth and creativity within the field. Because various countries have distinct laws governing cosmetics, it can be difficult to maintain uniformity around the world. Several efforts have been made to expedite international commerce and unify regulatory frameworks globally in order to overcome these issues. The EU's member nations, for instance, all follow the same laws. Cosmetic law is ultimately governed by legal (EC) No. 1223/2009 of the European Commission, which creates the legal framework for cosmetics. The relevant authority of each member state then puts it into practice (55). Other regions haven't yet seen this type of development, though. For instance, Under the direction of the Food and Drug Administration (FDA), the two most important laws governing cosmetics in the US are the Federal Food, Drug and Cosmetic Act (FD&C Act) and the Fair Packaging and labelling Act (FPLA). With relatively minor modifications, these statutes, which have been in effect since 1938 and 1966, respectively, have mainly stayed the same (56). The Food and Drugs Act of 1985 and the Cosmetic Regulation Act of 1977 have not altered much in Canada throughout the years, creating similar conditions (57). Alongside this general rule, a number of subsidiary regulations have been developed, especially those that concern, among other things, adverse reaction monitoring, good manufacturing procedures (GMPs), and the registration and reporting procedure (58).

SAFETY ASSESSMENT OF NANO COSMETICS

Skin and Eye Corrosivity, Sensitivity, and Irritation

To screen for skin sensitivity the local lymph node test is frequently used and this is in vivo testing technique. It gauges how much the test chemical stimulates lymphocyte proliferation in lymph nodes following administration and inside this secondary lymphoid organ. A vital cellular defense mechanism, the Keap1-Nrf2-ARE system (Kelch-like ECH-associated protein 1)-Nrf2 (nuclear factor-erythroid 2-related factor 2)-ARE) is triggered in response to oxidative/electrophilic stress. This activation is measured by the ARE-Nrf2 skin sensitization test, an in vitro reporter gene test. Its ability to cause skin sensitization may be predicted using it. The KeratinoSensTM test technique (reporter cell line) is used in the test (59). Additional research demonstrates its potential use in photo safety testing evaluations (60). Another helpful technique is the h-CLAT, which examines and measures dendritic cell activation. As an "in chemico" test for evaluating skin sensitization, the

direct peptide reactivity test measures the phenomenon of haptenation, which is the process by which small molecules bind to larger molecules and become immunogenic as a result of the active ingredient in cosmeceuticals interacting with certain proteins (amino acid residues) (60).

Skin permeability

Determining cosmetic risk also requires evaluating the rate of skin absorption. Systemic exposure is evaluated using this method. The rate of skin absorption of cosmetic chemicals was assessed using in vivo techniques (OECD Test No. 427). However, at the moment, cosmetic chemicals can only be used in vitro with human or pig skin. Research Committee on Consumer Safety (SCCS) 2020a; OECD Test No. 428. Several conditions must be met in order to evaluate skin absorption in vitro. Franz diffusion cells, also known as static diffusion cells, are among the most often used tools for in vitro skin penetration tests. Flow-through cells and static diffusion cells are the two primary cell types utilized in in vitro treatments. A sample of static diffusion cells is removed from the receptor-containing compartment at each time point, and fresh receptor fluid is added (61). Static diffusion cells have two benefits over flow-through cells: they are less expensive and have a simpler design. They provide a variety of surface areas to facilitate skin exposure testing (8). It has been shown that in order to maintain physiological conditions, flow-through cells continuously gather the perfusion fluid and continuously provide the receptor fluid (61). Additionally, requirements are needed for a number of situations, including the minimum number of repeats and sample quantity. It is crucial to confirm the various requirements listed in the SCCS (2020a) standards and the OECD (Test No. 428).

Geno toxicity

The Genotoxicity test involves the use of both in vitro and in vivo testing. The Scientific Committee for Consumer Safety (SCCS) suggests some requirements for in vitro geno toxicity testing (62). Two Geno toxicity tests are advised by SCCS for substances used in cosmetics. The in vitro micronucleus test evaluates chromosomal abnormalities (aneugenicity) and structural abnormalities (clastogenicity), whereas the Ames test evaluates gene alterations. Thus, four scenarios are produced by the Geno toxicity test results for cosmetic components. First, if the results of the Ames and in vitro micronucleus tests are negative, meaning that the test product is not deemed genotoxic, then no more testing is necessary. Second, the test material is deemed an in vitro mutagen if the Ames test is negative and the in vitro micronucleus test is positive; additional testing is required to determine the test substance's clastogenic potential. Third, the test substance is categorised as an in vitro mutagen if the Ames test is positive and the in vitro micronucleus test is negative. Additional research, including an in vitro gene mutation test, could be required. Fourth, additional verification studies are

not required if both trials yield positive results, indicating that the test material has the potential to be mutagenic (63).

Carcinogenicity

Many investigations and analyses are carried out to determine whether the usage of hair color contributes to the occurrence of any particular type of cancer. After a review of the literature on epidemiological studies, it was established that there was evidence, based on a number of results, that personal use of hair coloring agents was linked to a higher risk of breast tumor (8 case-control) (64). Another 2015 case-control research discovered a link with the occurrence of cancer and the use of hair color (65). After research revealed a rise in bladder cancer incidence among professionals (hairstylists and barbers), more research was done on the subject of personal usage; the results are either unclear or left room for discussion (66).

Photo toxicity

It is necessary to assess cosmetic chemicals for the level of skin damage they cause after being exposed to light. Common cosmetic components that are linked to skin damage and light exposure include preservatives, hair colors, and UV filters. Using the 3T3 fibroblast cell line, the in vitro photo toxicity approach is predicated on the uptake of neutral red. After validation, it was added to the list of OECD test guidelines (OECD test no. 432) (67).

CONCLUSION

As we can see, the nanoparticles size has a significant impact on their ability to enter the systemic circulation and followed by reaching and accumulation of these particles into the various organs of the body. As we deal in nanoscale parameters the important part for the formulators is the size of the particles should not be small beyond the limit that it can facilitate more penetration and can induces the various types of toxicities. Numerous regulatory bodies are essential in ensuring that certain nanomaterials are avoided in excess and do not cause toxicity; in fact, several nations have prohibited some harmful nanomaterials.

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